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Practice of Epidemiology

Variation in Mortality Patterns Among the General Population, Study Participants, and Different Types of Nonparticipants: Evidence From 25 Years of Follow-up

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Abstract
The general willingness to participate in health surveys is decreasing, resulting in increasingly selected study populations. We aimed to examine relative mortality rates by different categories of nonparticipation. We included 14,223 men and women aged 25–74 years who were sampled in the Swiss centers of the international Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Study (1983–1992) and followed-up until 2008. Logistic regression was used to describe factors associated with nonparticipation. We compared persons who refused to participate (n = 2,911), persons who did not go to their examination (n = 470), and persons that could not be contacted for inclusion in the MONICA Study (n = 989) with participants (n = 9,853). We used Cox regression to determine mortality hazard ratios for the various categories of nonparticipants versus participants or versus the 1990 Census population average. Persons who refused were more likely to be older and female. Compared with participants, those who refused had a higher risk of death (for men, hazard ratio = 1.34, 95% confidence interval: 1.17, 1.54; for women, hazard ratio = 1.31, 95% confidence interval: 1.12, 1.52), whereas persons who did not go to their examination and those who could not be contacted did not differ. Compared with the general (census) population, participants had a lower risk of all-cause mortality and those who refused had a higher risk of all-cause mortality. These variations were mainly due to cardiovascular disease and not cancer. Variations in relative mortality risks between study participants and the general population could depend on the proportion of subjects who actively refused to participate in the study. Considering the increasing participation reluctance, our findings underline the importance of carefully assessing the reasons for nonparticipation.

health survey; nonparticipation bias; refusal; study population; Swiss National Cohort

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; ICD, *International Classification of Diseases*; MONICA, Monitoring of Trends and Determinants in Cardiovascular Disease; SNC, Swiss National Cohort.

Limited study participation and the resulting selected study populations are known but as of yet unsolved problems. These problems might increase in the future because the proliferation of marketing surveys and political polls have created an "oversurveyed society" (1). The willingness of people to participate in health surveys may depend on sociodemographic factors, individual health characteristics (specific symptoms or conditions), or risk behaviors (1–3).

For most epidemiologic research, representativeness is not essential for internal validity of relative effect measures (4). However, for public health applications (e.g., analyses of "structural" interventions or estimations of future health care demand), this may not be true. Absolute mortality risk estimates may be biased because of low participation rates if selection is associated with the outcome (1, 5). In such cases, absolute effect measures comparing the risk between 2 exposure groups will also be biased. Moreover, the relative effects of an exposure on the outcome of interest could be distorted if the exposure is associated with nonparticipation and occurred before selection into the study. However, evidence of the kind and size of the resulting bias is rather scarce and often conflicting. Nonparticipants have generally higher disease and mortality risks, poorer health status, and lower levels of functioning than do study participants (1, 6). Study populations generally have lower rates of all-cause mortality than the general population (7–10). However, it is controversial whether this mortality disadvantage persists for more than a few years of follow-up (3, 11). In any case, bias arising from the assumption that the study population is the same as the general population may be aggravated by an underestimation of relative risks (e.g., smoking vs. not smoking, obesity vs. normal weight) arising from a lower participation rate for individuals with poor health status/behavior from lower socioeconomic groups than for better-off groups (12, 13).

There are several reasons why the number of persons included in a study may be smaller than the sampled population: Individuals may not be contactable, may refuse to participate, or may not show up for examinations. Unfortunately, "response rate" is often not clearly defined, and full information on participation rates is often not reported (1). Even in recent publications from journals with high impact factors, nonparticipation is mostly ignored or dismissed (14). A rare example in which nonrespondents were distinguished into categories of subjects who were excluded, could not be contacted, refused to participate, and did not attend their examination is the Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Study, a multicenter project initiated by the World Health Organization (15).

Thanks to the record linkage with the Swiss National Cohort, our Swiss MONICA database offers an excellent opportunity to examine this issue because it has an exceptionally long follow-up period. Our aim was to compare all-cause and cause-specific mortality risks between persons who did and did not participate in the Swiss MONICA studies for different reasons and to analyze factors associated with participation status. Given the special focus of the MONICA Study, we additionally aimed to examine a possible specific impact of participation status on death from cardiovascular disease (CVD).

METHODS

MONICA data

In total, our database included 15,893 records from all 3 population studies conducted in Switzerland within the framework of the MONICA Study: MONICA I (1984–1986; n = 5,298), MONICA II (1988–1989; n = 5,296), and MONICA III (1992–1993; n = 5,299). The 2-stage sampling procedure, which was identical in all 3 study waves, consisted of 1) selecting a sample of 51 out of 651 communities after stratification according to their size and 2) selecting the subjects from the population files of the communities (resident population aged 25–74 years in Vaud/Fribourg and aged 35–64 years in Ticino; for details see Wietlisbach (16)). The selected persons were invited to attend a health examination in their community of residence and to complete a self-administered questionnaire. Response rates in Ticino were substantially higher than in Vaud/Fribourg (15), probably because of a broad CVD prevention campaign conducted there in the 1980s (17).

Of the 15,893 sampled individuals in our database, 348 (2.2%) were excluded because they died or moved out of the area before the beginning of the original study. Of the remaining 15,545 persons, 1,388 (8.9%) could not be contacted, 3,422 (22.0%) refused to participate, 572 (3.7%) didn't show up for the health examination, and 10,163 (65.4%) participated. In the first MONICA Study wave, sampled individuals from Ticino who were excluded or could not be contacted by phone were replaced by surplus samples (17). Of the 427 subjects who refused or who did not show up for the health examination during this study wave, 264 (62%) agreed to fill in a subsidiary questionnaire. Compared with participants, these nonparticipants reported substantially lower proportions of having been told by a physician that they have hypertension; however, their body mass indices and smoking behaviors were similar (17).

Swiss National Cohort data

The Swiss National Cohort (SNC) is a nationwide anonymized record linkage of census and mortality records that includes all residents of Switzerland enumerated in the national 1990 or 2000 census. Deterministic and probabilistic methods of record linkage were used to link anonymized census records to death or emigration records (18). Of the 6,874,000 persons registered in the census of December 4, 1990, 6.9% could not be linked to a census 2000 record, a death record from 1990 to 2000, or an emigration record from 1990 to 2000. Swiss census enumeration and registration of deaths that occurred in Switzerland (including information on cause of death) are virtually complete. Registration of deaths—but not necessarily of cause of death—of Swiss nationals abroad is expected to be quasi complete. In contrast, for foreign nationals who resided in Switzerland, registration of deaths that occurred abroad is incomplete.

Linkage of MONICA and SNC

Because some small communities were included in 2 or even 3 MONICA Study waves, it was possible that the same person was included more than once. As a preliminary step, all participants with the same sex, date of birth, and community were checked for repeated sampling (10).

Of the 15,545 MONICA participants and nonparticipants (those who refused, who did not go to their examination, or who were not contactable), 258 had an invalid date of birth, and an additional 42 nonparticipants appeared to have already been sampled in a preceding study wave, which resulted in 15,245 persons who were eligible for record linkage with the SNC. This enabled us to analyze a broad range of determinants for nonparticipation, as well as mortality differentials between the different groups of MONICA nonparticipants. Again we used record linkage procedures that included all potential (anonymous) identification variables (for details, see Bopp et al. (10)). The minimum required information for a promising linkage of MONICA and SNC records was sex, exact date of birth, and place of residence. Additional helpful identification variables were nationality and marital status, as well as educational category and profession for MONICA participants. Deaths that occurred before the 1990 census are not included in the standard SNC data and had to be evaluated separately for potential linkage. MONICA subjects who were not retraceable in the SNC, that is, data from the 1990 census, had to be evaluated separately for a potential link with the official death registry. Therefore, the rate of linkage for deaths that occurred before the 1990 census was expected to be lower.

Statistical analysis

We calculated means and percentages of various characteristics in different categories of participants and nonparticipants. We used logistic regression models to measure the association of factors with participation status, especially with respect to sociodemographic variables. To explore mortality differences between categories of participants and the general 1990 census population, we calculated Cox proportional hazards models that were adjusted for several confounding variables. The proportional hazards assumption was checked visually using Schoenfeld residuals. It was satisfactorily fulfilled for all covariates except sex; therefore, we fitted models with the partial likelihood stratified by sex. From a set of potential confounders described in the next section, we selected those that were the most suitable using the Bayesian information criterion for both Cox and logistic regression. We additionally used Cox models to compare the different participant categories with the general populations from the 1990 census in the respective study regions. Similarly, mortality risks by different causes of death (CVD, cancer, or other) were analyzed. For sensitivity analyses, we also calculated the Cox models for shorter follow-up periods. Persons with missing covariate values were excluded from the analysis when calculating the respective regression models. In the analysis of the different participant categories, the proportions of excluded values were 5.7% in women and 11.8% in men. For the comparison with the 1990 census population, 2.5% of men and 1.5% of women had to be excluded because of missing covariate values.

Exposure and outcome variables

Causes of death were classified according to the *International Classification of Diseases* (ICD), *8th* and *10th Revisions*. In Switzerland, the ICD-8 was used until 1994, and the ICD-10 was used thereafter. We examined deaths from CVD (ICD-8 codes 390–458 and ICD-10 codes I00–I99), cancer (ICD-8 codes 140–239 and ICD-10 codes C00–C99 and D00–D48), and noncancer, non-CVD causes (all other codes).

We examined the following potential explanatory variables and confounders in the process of choosing the most suitable models: sex, age (years), marital status (single, married, widowed, divorced), nationality (Swiss, other), region (Vaud/Fribourg, Ticino), study wave (I, II, III), home ownership (binary), household type (single, couples and families, other multiperson, institution), highest achieved educational level (number of years), principal personal language (German, French, Italian, other), relation of place of birth and place of residence in 1990 (same community, same canton, other canton, other country), occupational class (high,

middle, low, not working), employment (full time, part time, housewife, jobless, other), and religious affiliation (Protestant, Roman Catholic, none). All exposure variables could be assessed only at baseline.

RESULTS

In total, 14,223 MONICA samples could be linked to the SNC, including 9,853 of the 10,160 eligible participants (97%) and 4,370 of the 5,085 eligible nonparticipants (86%). The rate of linkage success for persons who refused (90%) and persons who did not go to their examination (86%) was somewhat higher than for persons who were not contactable (76%). Among the linked samples, nonparticipants, particularly those who could not be contacted, were more often not married, non-Swiss nationals, and residents of the Vaud/Fribourg region than were participants (Table 1), with persons who did not go to their examination generally having rates between those who refused and noncontactable persons.

Generally, the sociodemographic patterns in MONICA participants, nonparticipants, and the census populations of the regions covered by MONICA were quite similar (Web Tables 1 and 2, available at http://aje.oxfordjournals.org/). However, persons who refused to participate had a higher mean age at study entry, and when compared with participants, persons who did not go to their examinations, and person who could not be contacted, a larger percentage were female.

Table 2 shows the odds of being in 1 of the 3 nonparticipant categories versus being a participant. The odds of refusing to participate increased with each MONICA wave (for wave II, OR = 1.44; for wave III, OR = 1.78; $P < 0.001$ for both), and persons with a foreign nationality were generally more likely to not participate (for those who refused, OR = 1.20, $P = 0.007$; for those who did not show up for their examination, OR = 1.63, $P < 0.001$; and for those who could not be contacted, OR = 1.89, $P < 0.001$). Of notable interest is the significant odds of German speakers not going to their examinations (OR = 0.65; $P = 0.047$). Although German-speaking persons were significantly more likely to refuse to participate, they were also more likely to keep the promise to undergo a medical examination than were persons who spoke another language. As expected, persons who were single were less likely to participate, and homeowners were less likely to refuse or to not be contactable, probably because these persons move less frequently and therefore were easier to track.

Table 3 shows the association of belonging to different participation categories with the risk of all-cause mortality (also see the Kaplan-Meier curves in Web Figures 1 and 2). Those who refused showed a clearly elevated mortality risk, with a hazard ratio of 1.33. This applied to both men (hazard ratio (HR) = 1.34; 95% confidence interval (CI): 1.17, 1.54) and women (HR = 1.31; 95% CI: 1.12, 1.52). The mortality risk of persons who did not come to the arranged examination did not significantly differ from that of participants. A significant hazard ratio of 1.42 (95% CI: 1.12, 1.81) was found for men who could not be contacted but not for noncontactable women. These patterns persisted if we examined shorter follow-up times of 20, 15, or 10 years, but with slightly higher hazard ratios in most cases (data not shown). As suggested by Westreich and Greenland (19), we additionally calculated hazard ratios for the participant categories with models that included fewer covariates. The data in Web Table 3 show that changes of the estimates resulting from different combinations of covariates can be observed.

Table 4 shows that participants had a significant survival advantage compared with the general 1990 census population (for all-cause mortality, HR = 0.85, 95% CI: 0.80, 0.90). On the other hand, those who refused to participate had a significantly higher hazard ratio of 1.12 (95% CI: 1.03, 1.22) compared with the census population. However, this significant increase applied to men (Web Table 4) but not to women (Web Table 5). Alternative hazard ratios from competing models with fewer covariates can be found in Web Table 6.

Separate models for cause-specific mortality provided partly similar results (Table 4): Compared with the census population, participants had a significantly lower risk of death from CVD (HR = 0.88, 95% CI: 0.79, 0.98), and those who refused had a significantly higher risk (HR = 1.32, 95% CI: 1.14, 1.52). Among those who refused to participate, the risk elevation for death from CVD applied to both men (HR = 1.32, 95% CI: 1.08, 1.61) and women (HR = 1.35, 95% CI: 1.09, 1.67); however, the risk reduction among participants was limited to men (HR = 0.85, 95% CI: 0.74, 0.98).

In both sexes, the most pronounced risk decrease concerned the noncancer, non-CVD deaths among participants (for men, HR = 0.73, 95% CI: 0.62, 0.86; for women, HR = 0.71, 95% CI: 0.59, 0.86), whereas death from cancer among participants and those who refused virtually did not differ from the census population. Persons who did not go to their examination and persons who could not be contacted did not show any significant difference from the census population.

For sensitivity analyses, we calculated the Cox models with follow-up times of 10, 15, and 20 (instead of 25) years. The pattern remained similar, with slightly more distinctive results for persons who refused

participation or could not be contacted. In addition, the interaction terms of participation status and nationality or study wave were both statistically nonsignificant.

DISCUSSION

We looked at long-term survival rates of participants and persons who did not to participate in a Swiss CVD study for various reasons. We found intriguing differences by reason for not participating. Among the sampled persons, men and women who refused to participate and men who were not contactable had adjusted mortality risks that were between 31% and 42% higher than those of participants. In contrast, both men and women who agreed to participate but did not show up for examination and women who could not be contacted did not significantly differ from participants. Also, compared with the general population (1990 census) of the 2 study areas, male and female participants had a significantly lower adjusted mortality risk. Among men but not women, those who refused had a significantly higher mortality rate than did the census population.

Differences in survival between participants and nonparticipants have been found by others (7–9). Participants may be healthier than nonparticipants because they have a healthier lifestyle and fewer risk factors (1, 6). A part of this variation may also be explained by the lower socioeconomic status of nonparticipants (12). In the present study, the survival advantage of participants was visible over the entire follow-up time of 25 years, although in line with others (11), the effect size slightly decreased over time in most cases. Other studies had a shorter follow-up period, and some have questioned whether this mortality disadvantage persists for more than a few years (3, 11). Our results suggest that increasing the participation rate at all costs to optimize general population representativeness may not be sensible. Having a study sample that is representative of a total population (e.g., the entire population of Switzerland) could only be regarded as a worthwhile goal if the study is attempting to measure the effect of interventions that cover all residents, for example, a public smoking ban, improvement in walkability of neighborhoods, general salt reduction in food, increases in taxes on alcohol, or measures aimed at reducing air pollution. In contrast, if the aim is to assess the effect of a health promotion program, a high population coverage of the study may not be the most desirable because the number of persons accessible for such a program may also be limited. Rather, it would be preferable to have a study sample that is representative of the population that would be likely to receive the intervention.

When comparing CVD mortality rates with those for cancer, the more pronounced survival difference between participants and those who refused may be driven by the nature (CVD prevention) of the MONICA Study: Persons who have a particular symptom or condition or who attach personal relevance to a study are more likely to participate in relevant studies (1, 3, 20). More unexpected is the finding that the survival advantage of participants was even more pronounced for noncancer, non-CVD deaths. It could be speculated that for ethical reasons, pathological results discovered in the medical examination were disclosed to the participants. However, we could not find respective information in the MONICA literature on whether and (if so) how these persons were treated and counseled with regard to, for example, hypertension or dyslipidemia.

We were able to determine various properties of nonparticipants. In line with many other studies (1, 3, 7, 21), having a lower educational level and not living as couple/family was more prevalent among nonparticipants than among participants. A lower representation of foreign nationals has also been described (2). This general pattern also applies to those attended the medical examination; it is possible that persons who require less effort to travel to the study site (urban people) or who are more mobile (ages 25–49 years) are more likely to participate (2, 22). This is in line with the higher odds of refusing associated with increasing age in the present study. At variance with our study, female sex is generally associated with higher participation rates (1, 3, 7, 21). However, a lower rate of participation among women in the MONICA surveys was not at all exceptional, with approximately half of the MONICA centers reporting higher participation rates among men than among women (15). Generally, participation of women was lowest in the initial MONICA wave and in the oldest age group, whereas it was highest in the final wave and the 2 youngest age groups. It may therefore be speculated that because of the large difference in mortality and risk factors (e.g., smoking), particularly in the early 1980s, MONICA was perceived as addressing men more strongly than women. Another example of higher participation in men was reported from Denmark (23). However, only few studies differentiated between those who refused and those who were not contactable, with the latter generally more prevalent among men than women. Apart from MONICA, a study from Scotland also reported that women had higher odds of refusing to participate (24). In general, misestimation

of health outcomes potentially arising from sampled persons not who do not participate in the study is mostly neglected in epidemiologic journals, which could potentially lead to false conclusions (14).

Our study has several limitations. First, we were limited to mortality data because we had no available information on other health outcomes (e.g., prevalent/incident nonfatal diseases). We also had no information on variations in CVD risk factors by participation status. Survival can be regarded as an "end of life" measure of cumulative life-course exposure, and from a public health perspective it would be important to have more detailed information about the entire life course. Second, we cannot exclude the possibility that differential linkage success slightly biased the results. Whereas 97% of participants could successfully be linked to the SNC, rates of linkage success for persons who refused (90%), persons who did not go to their examination (86%), and persons who could not be contacted (76%) were somewhat lower. However, we found no indication of a selective impact because the most important reason for linkage failure was the exact date of birth being missing, and younger age was associated with more frequent changes of residence, making tracking of individuals difficult. Consequently, it is not surprising that the odds ratios for being a foreign national or for not living in a couple/family household were higher (and for being a homeowner lower) among noncontactable persons than among the other nonparticipants.

Our study stresses the importance of taking into account the fact that sampled men and women may not participate in studies for several reasons and that this may be significantly associated with estimations of absolute risk, as well as estimations of future health care demand and costs. Differences in mortality estimates between participants and the general population may depend on the disease-specific focus of the study. Mortality variations between participants and nonparticipants may be mainly driven by those who actively refuse to participate and much less by those who do not participate because they cannot be contacted or because they do not show up for the examination despite having agreed to participate.
Studies should provide results that allow the planning and implementation of effective public health interventions. However, it remains questionable whether a high general population representativeness is appropriate to achieve this aim or whether it is better for participants in studies to represent persons at whom programs for improving health behavior are aimed.

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Table 1. Proportions of Participants and Nonparticipants in Subjects From the Swiss Monitoring Trends and Determinants in Cardiovascular Disease Study (3 Waves, 1984–1993) Who Were Linked With the Swiss National Cohort (Until 2008)

Characteristics	% of Participants[a] (*n* = 9,853)	% Who Refused[b] (*n* = 2,911)	% Who Skipped Examination[c] (*n* = 470)	% Unable to be Contacted[d] (*n* = 989)
Male sex	50.4	45.9	48.9	51.4
Mean age, years	47.8	48.9	44.5	43.3
Marital status				
Single	12.3	15.4	18.3	28.6
Married	77.0	70.6	65.3	51.7
Widowed	4.0	6.0	3.8	5.7
Divorced	6.7	7.9	12.6	14.0
Swiss nationality	81.9	78.7	71.7	68.0
Ticino region	44.5	28.1	42.1	18.4
Study wave				
I	33.7	24.4	33.2	28.6
II	34.6	35.6	29.8	35.0
III	31.7	40.0	37.0	36.4

[a] *n* = 1,526 deaths.
[b] *n* = 635 deaths
[c] *n* = 62 deaths.
[d] *n* = 158 deaths.

Table 2. Factors Associated With Nonparticipation Versus Participation Based on Logistic Regression in Subjects From the Swiss Monitoring Trends and Determinants in Cardiovascular Disease Study (3 Waves, 1984–1993) Who Were Linked With the Swiss National Cohort (Until 2008)

Variable	Refused vs. Participated (*n* = 11,673)		Skipped Examination vs. Participated (*n* = 9,437)		Not Contactable vs. Participated (*n* = 9,905)	
	OR	95% CI	OR	95% CI	OR	95% CI
Study wave						
I	1.00	Referent	1.00	Referent	1.00	Referent
II	1.44	1.28, 1.61	0.86	0.67, 1.10	1.13	0.94, 1.35
III	1.78	1.59, 1.99	1.15	0.90, 1.45	1.26	1.05, 1.51
Region						
Vaud/Fribourg	1.00	Referent	1.00	Referent	1.00	Referent
Ticino	0.49	0.41, 0.58	1.01	0.69, 1.49	0.42	0.32, 0.56
Sex						
Male	1.00	Referent	1.00	Referent	1.00	Referent
Female	1.09	1.00, 1.20	1.05	0.86, 1.28	0.91	0.78, 1.05
Age, years	1.01	1.00, 1.01	0.97	0.96, 0.98	0.97	0.97, 0.98
Nationality						
Swiss	1.00	Referent	1.00	Referent	1.00	Referent
Foreign	1.20	1.05, 1.37	1.63	1.26, 2.11	1.89	1.55, 2.30
Language						
French	1.00	Referent	1.00	Referent	1.00	Referent
German	1.42	1.23, 1.64	0.65	0.43, 0.99	1.21	0.96, 1.53
Italian	0.99	0.82, 1.20	0.95	0.62, 1.45	0.66	0.49, 0.90
Other	1.25	1.00, 1.55	1.09	0.71, 1.69	1.24	0.93, 1.64
Educational level, years	0.95	0.93, 0.96	0.97	0.93, 1.01	0.93	0.91, 0.96
Household type						
Couples/families	1.00	Referent	1.00	Referent	1.00	Referent
Single person	1.27	1.12, 1.45	1.68	1.28, 2.20	2.19	1.82, 2.63
Other multiperson	1.35	1.02, 1.78	1.73	0.97, 3.09	2.14	1.44, 3.17
Institution	0.74	0.44, 1.23	1.73	0.78, 3.84	2.49	1.50, 4.14
Homeowner (owner-occupier)						
No	1.00	Referent	1.00	Referent	1.00	Referent
Yes	0.86	0.78, 0.95	0.86	0.69, 1.07	0.59	0.50, 0.70

Abbreviations: CI, confidence interval; OR, odds ratio.

Table 3. Relative All-Cause Mortality by Sex Based on Cox Regression in Subjects From the Swiss Monitoring Trends and Determinants in Cardiovascular Disease Study (3 Waves, 1984–1993) Who Were Linked With the Swiss National Cohort (Until 2008)

Variable	Men and Women[a,b] (*n* = 12,985)		Men (*n* = 6,214)		Women (*n* = 6,771)	
	HR	95% CI	HR	95% CI	HR	95% CI
Participation status						
Participated	1.00	Referent	1.00	Referent	1.00	Referent
Refused	1.33	1.20, 1.47	1.34	1.17, 1.54	1.31	1.12, 1.52
Skipped examination	1.02	0.77, 1.35	1.03	0.72, 1.47	1.00	0.63, 1.59
Not contactable	1.26	1.04, 1.51	1.42	1.12, 1.81	1.08	0.80, 1.45
Study wave						
I	1.00	Referent	1.00	Referent	1.00	Referent
II	0.96	0.86, 1.07	1.02	0.88, 1.17	0.89	0.75, 1.05
III	1.05	0.93, 1.19	1.12	0.96, 1.32	0.96	0.79, 1.16
Region						
Vaud/Fribourg	1.00	Referent	1.00	Referent	1.00	Referent
Ticino	0.90	0.82, 0.99	0.99	0.87, 1.12	0.79	0.68, 0.93
Years of age	1.10	1.10, 1.11	1.10	1.09, 1.11	1.10	1.10, 1.11
Nationality						
Swiss	1.00	Referent	1.00	Referent	1.00	Referent
Foreign	0.92	0.80, 1.05	0.92	0.78, 1.09	0.91	0.72, 1.14
Educational level, years	0.94	0.93, 0.96	0.94	0.92, 0.96	0.96	0.92, 0.99
Household type						
Couples/families	1.00	Referent	1.00	Referent	1.00	Referent
Single person	1.20	1.06, 1.34	1.19	1.00, 1.43	1.16	0.99, 1.36
Other multiperson	1.23	0.97, 1.55	1.17	0.85, 1.60	1.26	0.88, 1.82
Institution	1.56	1.06, 2.29	1.79	1.05, 3.04	1.42	0.81, 2.48

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a]Partial likelihood stratified by sex.
[b]Based on the period of 1990–2008. There were 1,177 deaths in men and 845 deaths in women (2,022 deaths total).

Table 4. Relative Cause-Specific Mortality (1990–2008) From Cox Regression[a] in the Swiss Monitoring Trends and Determinants in Cardiovascular Disease Study (1984–1993) That Was Linked With the Swiss National Cohort (*n* = 12,985) Versus the General Population (1990 Census, *n* = 697,411)

Variable	Cause of Death							
	All Causes (*n* = 118,386)		CVD (*n* = 38,688)		Cancer (*n* = 38,663)		Noncancer, non-CVD[b] (*n* = 33,309)	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Census population	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Participation status								
Participated	0.85	0.80, 0.90	0.88	0.79, 0.98	0.96	0.88, 1.05	0.72	0.64, 0.82
Refused	1.12	1.03, 1.22	1.32	1.14, 1.52	1.00	0.86, 1.16	1.12	0.95, 1.32
Skipped examination	0.91	0.70, 1.19	0.75	0.43, 1.32	1.35	0.94, 1.93	0.58	0.30, 1.13
Not contactable	1.04	0.88, 1.24	1.05	0.77, 1.45	1.12	0.84, 1.49	0.86	0.61, 1.22
Region								
Vaud/Fribourg	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Ticino	0.92	0.91, 0.94	1.00	0.98, 1.03	1.13	1.11, 1.16	0.73	0.71, 0.75
Age, years	1.10	1.10, 1.10	1.14	1.14, 1.14	1.08	1.08, 1.08	1.11	1.11, 1.11
Nationality								
Swiss	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Foreign	0.85	0.83, 0.86	0.74	0.71, 0.76	0.81	0.78, 0.83	0.81	0.78, 0.84
Educational level, years	0.96	0.95, 0.96	0.95	0.95, 0.95	0.96	0.96, 0.96	0.95	0.95, 0.95
Household type								
Couples/families	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Single person	1.20	1.18, 1.21	1.18	1.15, 1.21	0.98	0.95, 1.00	1.33	1.30, 1.37
Other multiperson	1.15	1.12, 1.19	1.13	1.07, 1.19	0.92	0.87, 0.98	1.37	1.29, 1.44
Institution	1.54	1.49, 1.59	1.59	1.51, 1.67	0.76	0.71, 0.83	2.27	2.16, 2.38

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio.
[a]Partial likelihood stratified by sex.
[b]That is, without injury and poisoning and deaths occurred abroad with missing cause of death.

Web Table 1. MONICA participants and non-participants linked with the SNC compared to the respective 1990 census population, Vaud/Fribourg, ages 25-74

	participants	refusers	no-shows	not contactables	1990 census
n population	5,464	2,092	272	807	560,518
Deaths until end of 2008	947	467	36	119	92,547
Sex (% male)	50.5	45.3	51.5	51.2	49.4
Nationality (% Swiss)	85.0	80.7	72.4	68.5	77.8
Mean age at baseline (years)	46.8	48.2	41.9	42.3	46.2
Housing (%)					
owner-occupier	40.7	36.8	27.2	23.6	34.2
tenant	58.6	62.7	71.7	75.0	64.0
Household type (%)					
Single-person	12.7	15.4	15.9	22.9	16.5
couples and families	84.5	81.4	80.0	70.5	77.1
other multi-person	2.0	2.4	3.0	3.9	3.8
institution	0.8	0.7	1.1	2.7	2.6
Years of education (mean)	11.7	11.1	11.6	11.2	11.7
Place of birth & place of residence in 1990 (%)					
same community	20.2	18.6	16.6	16.9	17.2
same canton	35.7	34.4	28.7	26.7	31.9
other canton	23.5	21.4	23.0	20.1	22.5
other country	20.7	25.6	31.7	36.3	28.4
Language (%)					
German	12.8	14.9	6.8	11.2	12.8
French	77.1	71.2	75.6	68.1	70.7
Italian	4.0	5.1	6.8	6.2	4.6
Occupational class (%)					
high	20.0	16.5	19.2	16.5	16.0
middle	28.3	22.6	31.6	27.8	26.0
low	17.9	21.2	23.3	27.5	21.5
no indication or not employed	33.8	39.7	25.9	28.2	36.5
Employment (%)					
full time	51.1	48.0	60.9	59.6	51.8
part time	16.2	13.4	15.0	13.9	13.1
homemaker	13.1	14.6	10.9	8.1	12.4
jobless	1.1	1.6	2.3	2.9	1.8
pensioner	18.6	22.4	10.9	15.5	20.9
Religious affiliation (%)					
protestant	45.9	40.2	35.1	34.6	40.4
roman catholic	46.2	51.0	50.2	51.8	50.5
none	6.0	6.7	3.5	9.1	7.5

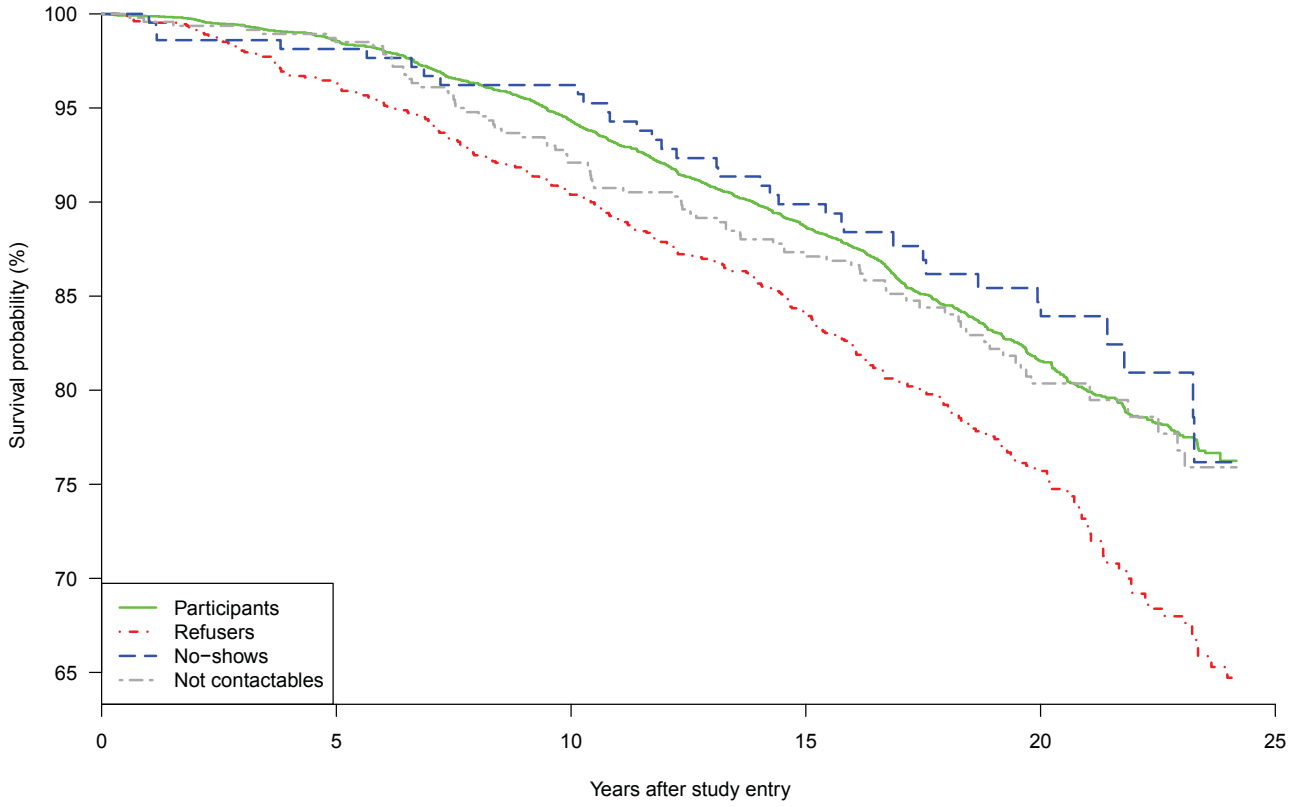
Abbreviation: MONICA: MONItoring trends and determinants in CArdiovascular disease; SNC: Swiss National Cohort

Web Table 2. MONICA participants and non-participants linked with the SNC compared to the respective 1990 census population, Ticino, ages 35-64

	participants	refusers	no-shows	not contactables	1990 census
n population	4,389	819	198	182	136,832
Deaths until end of 2008	579	168	26	39	18,583
Sex (% male)	50.3	47.5	45.5	52.2	48.2
Nationality (% Swiss)	78.2	73.8	70.7	65.4	73.4
Mean age at entry (years)	49.0	50.7	48.1	48.1	49.9
Housing (%)					
owner-occupier	50.9	40.7	43.5	24.6	44.9
tenant	48.5	59.0	56.0	73.7	54.2
Household type (%)					
single-person	10.0	15.4	18.0	25.6	13.5
couples and families	87.0	80.7	76.3	67.6	82.2
other multi-person	2.0	3.4	3.6	4.6	2.6
institution	0.9	2.1	2.1	2.3	1.8
Years of education (mean)	11.3	11.1	11.0	11.1	11.4
Place of birth & place of residence in 1990 (%)					
same community	23.4	21.0	19.7	14.3	19.9
same canton	31.3	26.2	29.0	19.4	27.7
other canton	12.4	15.5	7.8	18.3	14.3
other country	32.9	37.3	43.5	48.0	38.0
Language (%)					
German	9.3	14.5	6.7	19.8	11.7
French	2.4	2.1	2.6	2.8	2.3
Italian	86.1	81.3	86.6	71.8	81.4
Occupational class (%)					
high	20.9	19.6	15.5	20.9	18.2
middle	23.2	17.3	21.7	17.5	20.6
low	19.7	19.8	28.4	24.9	20.5
no indication or not employed	36.2	43.3	34.5	36.7	40.8
Employment (%)					
full time	52.0	48.0	53.1	54.8	49.4
part time	12.8	10.2	14.4	9.0	11.2
homemaker	21.5	20.2	19.6	15.3	19.9
jobless	0.5	0.9	0.0	0.6	1.2
pensioner	13.2	20.7	12.9	20.3	18.3
Religious affiliation (%)					
protestant	7.3	8.1	3.1	9.2	7.9
roman catholic	86.7	85.4	90.1	80.5	85.1
none	4.8	4.9	4.7	9.2	5.4

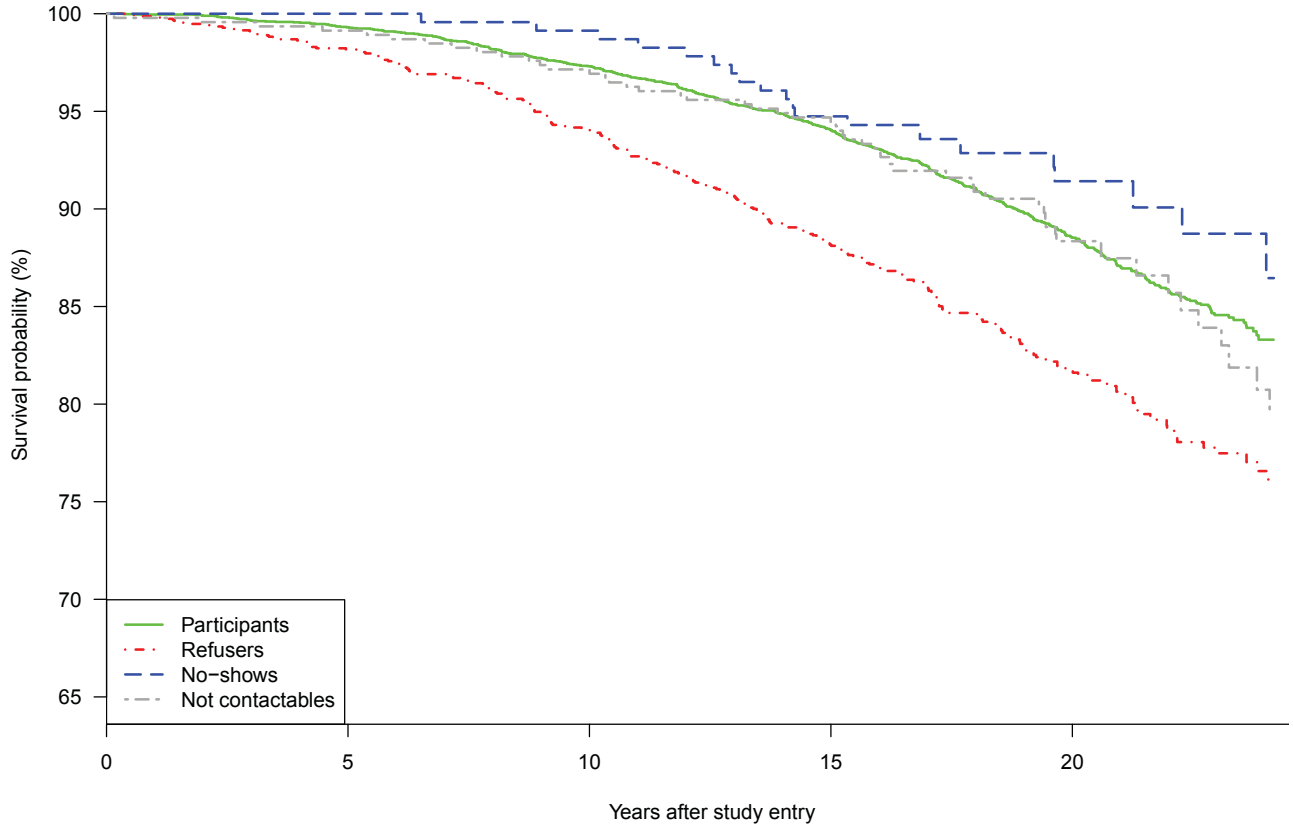
Abbreviation: MONICA: MONItoring trends and determinants in CArdiovascular disease; SNC: Swiss National Cohort

Web Figure 1. Kaplan-Meier survival curves by participation status, male MONICA participants and non-participants linked with the SNC



Abbreviation: MONICA: MONItoring trends and determinants in CArdiovascular disease; SNC: Swiss National Cohort

Web Figure 2. Kaplan-Meier survival curves by participation status, female MONICA participants and non-participants linked with the SNC



Abbreviation: MONICA: MONItoring trends and determinants in CArdiovascular disease; SNC: Swiss National Cohort

Web Table 3. (addendum to Table 3): Relative all-cause mortality based on Cox regression (partial likelihood stratified by sex), in the Swiss MONICA samples (1984-93) linked with the SNC (followed-up until end of 2008)

		Adjustment					
	Full*	age only	age + wave	age + region	age + nationality	age + education	age + household
Participation status							
participants (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
refusers	1.33	1.38	1.42	1.37	1.37	1.35	1.37
95% Confidence Interval	1.20, 1.47	1.26, 1.52	1.29, 1.56	1.25, 1.51	1.24, 1.50	1.22, 1.50	1.25, 1.52
no-shows	1.02	1.10	1.11	1.10	1.11	1.05	1.03
95% Confidence Interval	0.77, 1.35	0.85, 1.42	0.86, 1.43	0.86, 1.42	0.86, 1.43	0.80, 1.39	0.78, 1.35
not contactables	1.26	1.40	1.40	1.37	1.41	1.33	1.31
95% Confidence Interval	1.04, 1.51	1.19, 1.65	1.19, 1.66	1.16, 1.62	1.20, 1.66	1.11, 1.59	1.10, 1.57

*model used for Table 3

MONICA: MONItoring trends and determinants in CArdiovascular disease; SNC: Swiss National Cohort

Web Table 4. Relative cause-specific mortality 1990-2008 from Cox regression[a], Swiss MONICA samples (1984-93) linked with the SNC (n=6,214) vs. the general population (1990 census, n=340,039), men

	All-cause		CVD		Cancer		Non-cancer-non-CVD[b]	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
n deaths	*65,205*		*20,568*		*22,456*		*17,163*	
Population								
census (ref)	**1.00**		**1.00**		**1.00**		**1.00**	
participants	**0.85**	**0.79, 0.92**	**0.85**	**0.74, 0.98**	**0.97**	**0.87, 1.09**	**0.73**	**0.62, 0.86**
refusers	**1.14**	**1.02, 1.28**	**1.32**	**1.08, 1.61**	**0.99**	**0.81, 1.22**	**1.18**	**0.94, 1.48**
no-shows	**0.93**	**0.67, 1.31**	**0.88**	**0.46, 1.70**	**1.44**	**0.91, 2.26**	**0.55**	**0.23, 1.33**
not contactables	**1.11**	**0.89, 1.38**	**1.29**	**0.88, 1.89**	**1.26**	**0.89, 1.80**	**0.79**	**0.48, 1.30**
Age (years)	1.10	1.10, 1.10	1.12	1.12, 1.13	1.09	1.09, 1.09	1.10	1.10, 1.11
Nationality								
Swiss (ref)	1.00		1.00		1.00		1.00	
foreign	0.81	0.79, 0.83	0.69	0.66, 0.72	0.82	0.79, 0.85	0.77	0.74, 0.81
Education (years)	0.95	0.95, 0.95	0.95	0.95, 0.96	0.95	0.95, 0.96	0.95	0.94, 0.95
Household type								
couples/families (ref)	1.00		1.00		1.00		1.00	
single-person	1.25	1.22, 1.27	1.23	1.18, 1.28	1.01	0.97, 1.05	1.45	0.39, 1.51
other multi-person	1.12	1.07, 1.17	1.08	1.00, 1.17	0.86	0.79, 0.94	1.41	1.30, 1.53
institution	1.30	1.24, 1.37	1.36	1.25, 1.47	0.71	0.64, 0.79	2.03	1.88, 2.19
Region								
Vaud/Fribourg (ref)	1.00		1.00		1.00		1.00	
Ticino	0.95	0.93, 0.97	1.05	1.02, 1.09	1.12	1.09, 1.16	0.74	0.71, 0.77

[a] partial likelihood stratified by sex
[b] i.e., without injury and poisoning and deaths occurred abroad with missing cause of death
Abbreviation: CVD: cardiovascular disease; MONICA: MONItoring trends and determinants in CArdiovascular disease; SNC: Swiss National Cohort

Web Table 5. Relative cause-specific mortality 1990-2008 from Cox regression, Swiss MONICA samples (1984-93) linked with the SNC (n=6,771) vs. the general population (1990 census, n=357,372), women

	All-cause		CVD		Cancer		Non-cancer-non-CVD	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
n deaths	*53,181*		*18120*		*16207*		*16146*	
Population								
census (ref)	**1.00**		**1.00**		**1.00**		**1.00**	
participants	**0.84**	**0.77, 0.92**	**0.94**	**0.79, 1.12**	**0.94**	**0.82, 1.09**	**0.71**	**0.59, 0.86**
refusers	**1.10**	**0.97, 1.25**	**1.35**	**1.09, 1.67**	**1.01**	**0.80, 1.26**	**1.08**	**0.86, 1.37**
no-shows	**0.87**	**0.56, 1.35**	**0.53**	**0.17, 1.66**	**1.18**	**0.65, 2.14**	**0.63**	**0.24, 1.68**
not contactables	**0.95**	**0.72, 1.25**	**0.75**	**0.42, 1.33**	**0.92**	**0.57, 1.49**	**0.94**	**0.57, 1.54**
Age (years)	1.11	1.11, 1.11	1.16	1.16, 1.16	1.07	1.07, 1.07	1.12	1.12, 1.12
Nationality								
Swiss (ref)	1.00		1.00		1.00		1.00	
foreign	0.89	0.87, 0.92	0.78	0.73, 0.83	0.82	0.78, 0.87	0.85	0.80, 0.90
Education (years)	0.96	0.96, 0.97	0.94	0.93, 0.95	0.98	0.97, 0.99	0.96	0.95, 0.97
Household type								
couples/families (ref)	1.00		1.00		1.00		1.00	
single-person	1.13	1.11, 1.16	1.07	1.03, 1.10	1.04	1.00, 1.08	1.21	1.16, 1.25
other multi-person	1.15	1.11, 1.21	1.10	1.02, 1.18	1.05	0.97, 1.14	1.26	1.17, 1.36
institution	1.73	1.66, 1.81	1.67	1.56, 1.79	0.89	0.80, 1.00	2.35	2.20, 2.52
Region								
Vaud/Fribourg (ref)	1.00		1.00		1.00		1.00	
Ticino	0.89	0.88, 0.91	0.97	0.94, 1.01	1.14	1.10, 1.18	0.74	0.71, 0.77

* i.e., without injury and poisoning and deaths occurred abroad with missing cause of death

CVD: cardiovascular disease; MONICA: MONItoring trends and determinants in CArdiovascular disease; SNC: Swiss National Cohort

Web Table 6. (addendum to Table 4): Relative cause-specific mortality 1990-2008 from Cox regression (partial likelihood stratified by sex), in the Swiss MONICA samples (1984-93) linked with the SNC (n=12,985) vs. the general population (1990 census, n=697,411)*

		Adjustment				
	Full[#]	age only	age + nationality	age + education	age + household	age + region
	HR	HR	HR	HR	HR	HR
Population						
census (ref)	1.00	1.00	1.00	1.00	1.00	1.00
participants	0.85	0.84	0.83	0.83	0.85	0.85
95% Confidence Interval	0.80, 0.90	0.79, 0.89	0.79, 0.88	0.79, 0.88	0.80, 0.90	0.80, 0.90
refusers	1.12	1.12	1.12	1.11	1.14	1.13
95% Confidence Interval	1.03, 1.22	1.03, 1.22	1.03, 1.22	1.02, 1.21	1.04, 1.24	1.03, 1.23
no-shows	0.91	0.91	0.91	0.91	0.90	0.93
95% Confidence Interval	0.70, 1.19	0.70, 1.19	0.70, 1.19	0.69, 1.19	0.69, 1.17	0.71, 1.21
not contactables	1.04	1.12	1.12	1.09	1.08	1.11
95% Confidence Interval	0.88, 1.24	0.95, 1.33	0.95, 1.33	0.92, 1.29	0.91, 1.28	0.94, 1.32

* i.e., without injury and poisoning and deaths occurred abroad with missing cause of death
[#] model used for Table 4

MONICA: MONItoring trends and determinants in CArdiovascular disease; SNC: Swiss National Cohort